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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,351	11/16/2000	Ari Ayalon	1662/50302	6513

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EXAMINER	
STOCKTON, LAURA LYNNE	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,351	AYALON ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7-15,18 and 19* is/are withdrawn from consideration.

5)☒ Claim(s) *2* is/are allowed.

6)☒ Claim(s) *1, 3-6,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/3/06&2/27/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending in the application.

Election/Restrictions

Applicants' election without traverse of Group I in the response filed February 24, 2004 was acknowledged in a previous Office Action. The requirement was deemed proper and made FINAL in a previous Office Actions.

Claims 7-15, 18 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Election was made **without** traverse in the response filed February 24, 2004.

Rejections made in the previous Office Action that do not appear below have been overcome by Applicants'

amendments to the claims. Therefore, arguments pertaining to these rejections will not be addressed.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statements filed on February 3, 2006 and February 27, 2006.

Claim Objections

Claims 1, 3-6, 16 and 17 are objected to for being substantial duplicate of claim 2. When two claims in an application are duplicates, or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim. M.P.E.P. §706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the claims or the originally filed specification can be found for the phrase "diffraction peaks at 5.5 and 8.3 degrees 2θ" in currently amended claims 3 and 17. Applicants state that support is found for this amendment on page 5, lines 14-15. However, page 5, lines 14-15 state, "medium peaks at

5.3±0.2 and 8.3±0.2 degrees 2θ." Therefore, the claims lack written description as such.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

The nature of the invention

The nature of the invention is pharmaceutical compositions comprising Atorvastatin Form V or a hydrate thereof.

The state of the prior art

The state of the prior art is that it is known that many compounds exist in more than one crystalline form (polymorphs). Polymorphs exist in more stable and less stable (metastable) forms. The preparation of the pharmaceutical compositions requires creating solutions, milling, adding diluents, excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state, to resort

back to the most thermodynamically stable form, which is the form with the lowest vapor pressure. Polymorphs tend to convert from less stable to more stable forms (Rouhi, Chemical and Engineering News, February 24, 2003, pages 32-35, especially page 32). Drug companies must monitor the polymorph in the drug product to ensure that it persists during manufacture (Rouhi, page 34).

It is also the state of the prior art that an acceptable carrier for a pharmaceutical formulation can be water. Dissolving a specific crystalline form in water, creating an aqueous solution, would put the compound in its free form, and not in a crystalline form, with a specific X-ray diffraction pattern.

The predictability or lack thereof in the art

The predictability or lack thereof in the art is that a metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern and also that a

solution prepared from a specific crystalline form and water would contain the free form of the compound.

The amount of direction or guidance present and the presence or absence of working examples

While the specification has provided processes for the preparation of the Form V (see Example 1, for instance, on pages 13-14) and generic processes for preparing pharmaceutical compositions on pages 11-13, the specification fails to provide the steps of ensuring that the pharmaceutical compositions will maintain the specific forms as found in the specification and will not resort back to the free form or the most thermodynamically stable form of the compound.

The breadth of the claims

The breadth of the claims embraces a pharmaceutical composition comprising a therapeutic amount of atorvastatin Form V or hydrates thereof.

The quantity of experimentation needed

One of ordinary skill in the art would be unable to maintain a specific metastable crystalline form upon preparation into a pharmaceutical composition which may require milling or the formation of a solution. Therefore, the quantity of experimentation needed is undue.

The level of the skill in the art

While the level of skill in the art is high, one of ordinary skill in the art would be unable to maintain a specific metastable crystalline form upon the preparation of a pharmaceutical composition without direction and guidance that is not found in the instant specification. One of skill in the art would expect the pharmaceutical composition to contain the free form of the compound or the most thermodynamically stable form.

Response to Arguments

Applicants' arguments filed February 3, 2006 have been fully considered. Applicants argue that the plain meaning of the language of claim 16 is being ignored and that claim 16 is not being interpreted in a reasonable manner in light of the specification. Applicants argue that the stability argument is based on limitations that are not present in claim 16 by requiring that the pharmaceutical composition defined by claim 16 must contain crystalline Form V for some unspecified time, contain some unspecified proportion of crystalline Form V and/or be prepared by some particular process.

All of Applicants' arguments have been considered but have not been found persuasive. Instant claim 16 is directed to a pharmaceutical composition that is a solid or suspension comprising atorvastatin calcium Form V or hydrates thereof. In the instant specification on page 12, solid compositions and liquid

suspensions are discussed. As stated above, the preparation of the pharmaceutical compositions requires creating solutions, milling, adding diluents, excipients, surfactants, etc. Applicants have not shown that any of the atorvastatin calcium Form V or hydrates thereof would be present after undergoing a process such as milling in making a solid composition such as a tablet for a pharmaceutical use. Applicants have not disclosed any other process in making a solid composition. Therefore, Applicants' arguments are not persuasive.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim

the subject matter which applicant regards as the invention.

Claims 1, 3-6, 16 and 17 are rejected for being substantial duplicates of claim 2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Briggs et al. {WO 97/03959} or McKenzie et al. {WO 97/03958}.

Briggs et al. disclose, for example Form II, which has X-ray power diffraction patterns (see pages 5-6) and ^{13}C nuclear magnetic resonance chemical shifts (see

page 7) embraced by the instant claimed invention (see especially instant claims 3 and 5).

McKenzie et al. disclose Form III, which has X-ray power diffraction patterns (see page 4) and ^{13}C nuclear magnetic resonance chemical shifts (see page 5) embraced by the instant claimed invention (see especially instant claims 3 and 5).

Response to Arguments

Applicants' arguments filed February 3, 2006 have been fully considered. Applicants argue the differences between the X-ray power diffraction patterns and ^{13}C nuclear magnetic resonance chemical shifts in each of the cited references. In response, because of the processing required to make a solid composition, the pharmaceutical composition will contain other forms of atorvastatin calcium. See the instant specification on pages 13, lines 4-6. Applicants' arguments state, "claim 16 does not contain

any limitations with respect to the crystalline forms maintaining their structure for any particular length of time." (page 11 of Remarks section). Therefore, claim 16 is anticipated by the cited prior art.

Allowable Subject Matter

Claim 2 is allowed over the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact

the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
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May 1, 2006